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Subject: HPV Robust Summaries/Test Plan

For the HPV Program, attached in Word format are the test plan and robust summaries for Acetonitrile, 2,2',2'',2'''-(1,-ethane-diylidinitrilo)tetrakis- CAS# 5766-67-6, submitted by Akzo Nobel Functional Chemicals LLC. The commitment letter to the HPV Program is dated 11/23/99. An Internal Agency Tracking Number on the EPA website is 201-01415.

Thanks.

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**EDTN
HPV TEST PLAN**

Submitted to the U.S. Environmental Protection Agency

By

**Akzo Nobel Functional Chemicals LLC
December 2002**

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SUMMARY

Akzo Nobel Functional Chemicals LLC has sponsored ethylenediaminetetraacetonitrile (CAS# 5766-67-6), also known as EDTN, in the U.S. EPA High Production Volume (HPV) program. Although there are no experimental data on SIDS endpoints for EDTN, data exists on these endpoints for propylenediaminetetraacetonitrile (CAS# 110057-45-9), also known as PDTN and an analog of EDTN. This document will identify EDTN as a closed system intermediate making it exempt in the HPV program from testing of some SIDS endpoints and justify the use of PDTN data.

Robust summaries of studies on PDTN and EDTN are included in this submission. Data on EDTN from the EPIWIN computer model were used in the absence of experimental values on PDTN for boiling point, photodegradation and fugacity. EDTN data were also used to compare with PDTN experimental values for other environmental chemistry endpoints to show similarities between the two chemicals and support the use of PDTN data for mammalian toxicity and ecotoxicity endpoints. The table below summarizes the endpoints of interest in the HPV program, the available data, and indicates proposed testing.

Endpoint	Data Available & Sufficient	Testing Proposed
Physical/Chemical Characteristics	Yes	No
Photodegradation	Yes	No
Hydrolysis	Yes	No
Biodegradation	Yes	No
Transport	Yes	No
Acute Fish Toxicity	Yes	No
Acute Daphnia Toxicity	Yes	No
Acute Alga Inhibition	Yes	No
Acute Toxicity	Yes	No
Genetic Toxicity	Yes	No
Repeated Dose	Yes	No
Reproductive Toxicity	N/Ap	N/Ap
Developmental Toxicity	No	Yes

N/Ap – Not applicable

1.0 INTRODUCTION

Akzo Nobel Functional Chemicals LLC has sponsored EDTN (CAS# 5766-67-6) in the U.S. HPV program to assess its health and environmental hazards, including selected physical/chemical characteristics. In the absence of data on EDTN, data on the structurally similar chemical, PDTN (CAS# 110057-45-9), will be used.

This document includes identification of EDTN as a closed system intermediate and justification for the use of PDTN data. The justification for the latter is based on similarities in chemical structure, physical/chemical properties and metabolism between EDTN and PDTN. In addition, an evaluation of the available toxicity data and proposed test plan are included.

It is proposed that a developmental toxicity study be conducted on EDTN.

2.0 EDTN: A CLOSED SYSTEM INTERMEDIATE

EDTN, which is an intermediate in the production of EDTA, is synthesized by a reaction of 1,2 ethylenediamine, formaldehyde and cyanide. In this process, a ratio of four moles of formaldehyde and cyanide to one mole of 1,2 ethylenediamine are used.

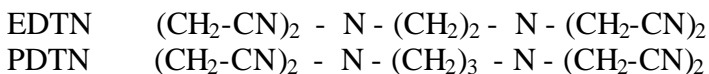
EDTN is manufactured at an Akzo Nobel facility in the U.S. and transported for use as an intermediate to three sites, two of which are outside the U.S. EDTN is transported in reusable large bags (woven polypropylene, UV stabilized, dust free seams) by trucks within the U.S. with the bags properly labeled with product safety information. At the EDTA production sites, the bags containing EDTN are stored in a warehouse. When needed for synthesis of EDTA, EDTN is transported by forklift from the warehouse to the manufacturing plant where the large bags are emptied into a reactor. In the reactor, a slurry is made of EDTN and water and then EDTN completely reacts in an alkaline environment to produce EDTA.

EDTN is a wet cake so the risk of worker exposure is low. However, plant operators wear masks and gloves to further reduce any chance of exposure. The bags are returned to the U.S. manufacturing facility to be used again. When the bags can no longer be used, they are sent to a recycling facility. The waste from the reactor following production of EDTN in the U.S. is sent to an EPA approved deep well at the manufacturing site. The waste from the reactor contains approximately 0.03% of EDTN.

Although measurements for residual levels of EDTN in EDTA have not been done, it is extremely unlikely that EDTN will be found in EDTA. EDTN is hydrolyzed in caustic during the production of EDTA with all nitrile groups of EDTN reacting during the process. This is followed by addition of an inorganic acid to EDTA at high temperatures resulting in a final product pH of less than 2.

3.0 PDTN: AN ANALOG

The structures of EDTN and PDTN are seen below.



The structures show that the only difference is that PDTN has one more carbon atom between the two nitrogens. Both chemicals have four identical acetonitrile groups which determine the function and reactivity of EDTN and PDTN. Due to the similarity, it is not unexpected that EDTN and PDTN have similar physical/chemical properties. Both are white solids with similar solubility in many types of solvents and have the same thermographic analysis curve. In addition, EDTN and PDTN react almost identically with water, ammonia, alkali, hydrogen and halogens.

The difference in synthesis of EDTN and PDTN is that 1,3 propylenediamine is used for PDTN unlike 1,2 ethylenediamine as described for EDTN above. PDTN is also used as a chemical intermediate. Table 1 compares the physical/chemical properties of EDTN and PDTN.

The similarity in structure, physical/chemical properties and reactivity suggests that the metabolism of EDTN and PDTN will be the same. In both cases, the bond between nitrogen atom and carbon atoms (N-CH₂-CN) can be broken by hydrolysis whereas the bridge, (N-(CH₂)₂-N) or (N-(CH₂)₃-N), is very stable. Therefore, the additional carbon atom in PDTN is not expected to change its metabolism relative to EDTN. The same metabolic pathway of EDTN and PDTN indicates that the toxicity profile of these structurally similar chemicals is expected to be the same. Therefore, the use of PDTN toxicity data for EDTN data gaps should be acceptable.

4.0 EVALUATION OF EXISTING DATA AND PROPOSED TESTING

The available data for PDTN and EDTN have been evaluated below and summarized in Tables 1-3. Since there are no experimental data on EDTN, the experimental data are only from studies on PDTN. Data on EDTN from the EPIWIN computer model were used in the absence of experimental values on PDTN for boiling point, photodegradation and fugacity. EDTN data were also used to compare with PDTN experimental values for other environmental chemistry endpoints to show similarities between the two chemicals and support the use of PDTN data for mammalian toxicity and ecotoxicity endpoints. Robust summaries of the studies are included in this submission. The Klimisch reliability code was used in the robust summaries. A literature search of online data bases including TOXLINE, HSDB and RTECS was searched. There were no studies identified for EDTN or PDTN.

Physical/Chemical Properties:

The melting point for PDTN is 73-74°C. The boiling point using the EPIWIN model for EDTN is 427°C. The density of PDTN is 1.23 g/cm³. The vapor pressure of PDTN is 1.43×10^{-3} mmHg at 20°C. The log octanol:water partition coefficient (log Kow) of PDTN is -1.3. The water solubility of PDTN is 1.67 g/L. The EPIWIN model for EDTN shows a melting point of 159°C, vapor pressure of 7.54×10^{-8} mmHg at 25°C, a log Kow of -2.17 and water solubility of 1000 g/L. These values for EDTN are consistent with the experimental values of PDTN.

Recommendation: No additional testing is proposed.

Environmental Fate:

AOPWIN was used to estimate the chemical half-life based on an overall OH reaction rate constant. Photodegradation modeling results for EDTN indicate the half-life is estimated to be 4.6 hours.

The hydrolysis half-life of PDTN at pH 4, 7, and 9 at 25°C is estimated to be 5.3, 3.9 and 0.3 years, respectively, based on data at higher temperatures. The EPIWIN model indicates that a hydrolysis half-life cannot be estimated for EDTN at 25°C which is consistent with the experimental data on PDTN.

The EPIWIN Level III fugacity model was used to estimate the distribution of EDTN. The modeling results indicate that EDTN primarily distributes to water and soil.

PDTN was biodegraded 0% at day 28 of a Modified Sturm Test. It is considered not readily biodegradable.

Recommendation: No additional testing is proposed.

Aquatic Toxicity:

The 96 hour LC50 in fish and 48 hour EC50 in *Daphnia magna* for PDTN are greater than 100 mg/L. The 72 hour EC50 for growth inhibition in algae for PDTN is 60 mg/L.

Recommendation: No additional testing is proposed.

Acute Toxicity:

The acute oral and dermal LD50 values in rats for PDTN are greater than 2000 mg/kg. PDTN was not irritating to rabbit skin following a 4 hour exposure and was not sensitizing to guinea pigs in a maximization test.

Recommendation: No additional testing is proposed.

Repeated Dose:

The NOAEL for PDTN in a 28 day oral gavage study in rats was 200 mg/kg/day. At 1000 mg/kg/day, increased liver weight and microscopic changes in the liver were reported.

Recommendation: No additional testing is proposed.

Reproductive/Developmental Toxicity:

There are no reproductive/developmental toxicity data on EDTN or PDTN. A reproductive toxicity study is not required since EDTN is a closed system intermediate.

Recommendation: A teratology study (OECD 414) is proposed for EDTN.

Mutagenicity:

PDTN was not mutagenic in the Ames test or clastogenic in cultured peripheral human lymphocytes in the presence and absence of metabolic activation.

Recommendation: No additional testing is proposed.

TABLE 1: PHYSICAL/CHEMICAL DATA

CAS #	Chemical (Mol. Weight)	MW	MP °C	BP °C	Vapor pressure (mmHg)	Water Sol. (mg/L)	Log Kow	Phys. Appear.
5766-67-6	EDTN (216)	216	159 ^a	427 ^a	7.54x10 ^{-8a} @25°C	1000000 ^a @25°C	-2.17 ^a	White crystalline solid
110057- 45-9	PDTN (230)	230	73-74	No Data	1.43x10 ⁻³ @20°C	1670 @18°C	-1.3	White crystalline solid

^a Data from EPIWIN

TABLE 2: SUMMARY OF ENVIRONMENTAL FATE AND ECOTOXICITY DATA

CAS #	Chemical (Mol. Weight)	Environmental Fate				Ecotoxicity LC50/EC50 (mg/L)		
		Photodeg (hr.).	Stability in water (25°C)	Biodeg.	Trans./ Distr.	Fish	Invert.	Plants
5766-67-6	EDTN (216)	4.6 ^a	No Data	No Data	Primarily to soil/water ^a	No Data	No Data	No Data
110057- 45-9	PDTN (230)	No Data	5.3 (pH 4), 3.9 (pH 7) and 0.3 (pH 9) years	Not readily biodegrad.	No Data	>100	>100	60 (growth); 129 (rate)

^a Data from EPIWIN

TABLE 3: SUMMARY OF MAMMALIAN TOXICITY DATA

CAS #	Chemical (Mol. Weight)	Genetic toxicity					
		Acute	Repeated dose	Reproductive	Develop.	Mutagen.	Chrom. Aberr.
5766-67-6	EDTN (216)	No Data	No Data	N/Ap	Test	No Data	No Data
110057- 45-9	PDTN (230)	>2 g/kg (oral/ dermal)	NOAEL – 200 mg/kg/day	No Data	No Data	Not mutagenic	Not clastogenic

N/ap – Not applicable for closed system intermediates

Test – OECD 414 study to be done



Safety,
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Environmental,
and
Regulatory
Affairs

EDTN
HPV Robust Summaries
Akzo Nobel Functional Chemicals LLC
December 2002

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1. Substance Information

CAS Number: 5766-67-6

Chemical Name: Acetonitrile, 2, 2', 2'', 2'''-(1,2-ethanediyldinitrilo) tetrakis-

Structural Formula: C₁₀H₁₂N₆

Other Names: Acetonitrile, (ethylenedinitrilo) tetra-; EDTN

Exposure Limits: None

2. Physical – Chemical Properties

2.1. Melting Point:

Identity: PDTN; CAS# 110057-45-9; Batch JNN98038

Method: OECD 102

GLP: Yes

Year: 1998

Value: 73-74°C

Decomposition: At temperatures above 231°C

Conclusions: The melting point of PDTN is 73-74°C.

Reliability: 1

Reference: 1

Remarks: None

Additional: None

References for Melting Point Studies:

Identity: EDTN; CAS# 5766-67-6

Method: EPIWIN Computer Model

GLP: Not applicable

Year: Not applicable

Value: 159°C

Decomposition: Not available

Conclusions: The melting point of EDTN is estimated to be 159°C.

Reliability: 1

Reference: 2

Remarks: None

Additional
References for
Melting Point
Studies: None

2.2. Boiling Point:

Identity: EDTN; CAS# 5766-67-6
Method: EPIWIN Computer Model
GLP: Not applicable
Year: Not applicable
Value: 427.17°C
Decomposition: Not available
Conclusions: The boiling point of EDTN is estimated to be 427.17°C.
Reliability: 1
Reference: 3
Remarks: None
Additional
References for
Melting Point
Studies: None

2.3. Density:

Identity: PDTN; CAS# 110057-45-9; Batch JNN98038
Method: OECD 109
GLP: Yes
Year: 1998
Value: 1.23 g/cm³
Conclusions: The density of PDTN is 1.23 g/cm³.
Reliability: 1
Reference: 4
Remarks: None
Additional
References for
Density Studies: None

2.4. Vapor Pressure:

Identity: PDTN; CAS# 110057-45-9; Batch JNN98038
Method: OECD 104
GLP: Yes

Year: 1998
 Value: $0.19 \pm 2 \text{ Pa} = 1.43 \pm 0.15 \times 10^{-3} \text{ mmHg}$
 Temperature° C: 20
 Pressure Unit: Pa or mmHg
 Decomposition: No
 Conclusions: The vapor pressure of PDTN at 20°C is $0.19 \pm 2 \text{ Pa} = 1.43 \pm 0.15 \times 10^{-3} \text{ mmHg}$.
 Reliability: 1
 Reference: 5
 Remarks: Static technique was used in the study
 Additional: None
 Reference for Vapor Pressure Studies:

Identity: EDTN; CAS# 5766-67-6
 Method: EPIWIN Computer Model
 GLP: Not applicable
 Year: Not applicable
 Value: $7.54 \times 10^{-8} \text{ mmHg}$
 Temperature° C: 25
 Pressure Unit: mm Hg
 Decomposition: Not available
 Conclusions: The vapor pressure of EDTN at 25°C is estimated to be $7.54 \times 10^{-8} \text{ mmHg}$.
 Reliability: 1
 Reference: 6
 Remarks: None
 Additional: None
 Reference for Vapor Pressure Studies:

2.5. Partition Coefficient (log Kow):

Identity: PDTN; CAS# 110057-45-9; Batch JNN98038
 Method: 107
 GLP: Yes
 Year: 1998
 Log Kow: -1.3

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Temperature°C: 40
 Conclusions: The log Kow of PDTN is -1.3.
 Reliability: 1
 Reference: 7
 Remarks: None
 Additional: None
 References for
 Partition
 Coefficient Studies:

Identity: EDTN; CAS# 5766-67-6
 Method: EPIWIN Computer Model
 GLP: Not applicable
 Year: Not applicable
 Log Kow: -2.17
 Temperature°C: Not available
 Conclusions: The log Kow of EDTN is estimated to be -2.17.
 Reliability: 1
 Reference: 8
 Remarks: None
 Additional: None
 References for
 Partition
 Coefficient Studies:

2.6. Water Solubility:

Identity: PDTN; CAS# 110057-45-9; Batch JNN98038
 Method: 105
 GLP: Yes
 Year: 1998
 Value at
 temperature°C: 1.67g/L at 18±1.5°C
 Description of
 solubility: Clear
 PH value and
 concentration at
 temperature °C: 7.8-8.1 at 18±1.5°C

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Pka value at 25°C: Not reported
 Conclusions: The water solubility of PDTN is 1.67 g/L.
 Reliability: 1
 Reference: 9
 Remarks: None
 Additional: None
 References for Water Solubility Studies:

Identity: EDTN; CAS# 576-67-6
 Method: EPIWIN Computer Model
 GLP: Not applicable
 Year: Not applicable
 Value at 1000 g/L at 25°C
 temperature°C:
 Description of solubility: Not available
 PH value and concentration at temperature °C: Not available
 Pka value at 25°C: Not available
 Conclusions: The water solubility of EDTN is estimated to be 1000 g/L.
 Reliability: 1
 Reference: 10
 Remarks: None
 Additional: None
 References for Water Solubility Studies:

3. Environmental Fate

3.1. Photodegradation:

Identity: EDTN; CAS# 5766-67-6
 Method: EPIWIN Computer Model
 GLP: Not applicable
 Type: Not applicable
 Year: Not applicable

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Light Source:	Not applicable
Light Spectrum (nm):	Not applicable
Half-life:	4.589 hours
Breakdown Products:	Not available
Conclusions:	The half-life in the atmosphere for EDTN is estimated to be 4.589 hours.
Reference:	¹¹
Remarks:	None
Additional	None
References for Photodegradation Studies:	

3.2. *Stability in Water:*

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038
Method:	EEC Directive 92/69, Part C Publication L383 1992
GLP:	Yes
Type:	Hydrolysis as a function of pH
Year:	1999
Half-life at a specific pH:	pH 4: 5.3 years at 25°C pH 7: 3.9 years at 25°C pH 9: 0.3 years at 25°C
Breakdown Products:	Not determined
Conclusions:	The half-life of PDTN at pH 4, 7 and 9 at 25°C is 5.3, 3.9 and 0.3 years, respectively.
Reliability:	¹
Reference:	¹²
Remarks:	Half-life at 25°C estimated from data of studies at higher temperatures.
Additional	None
References for Stability in Water Studies:	

3.3. *Transport (Fugacity):*

Identity:	EDTN; CAS# 5766-67-6
Method:	EPIWIN Computer Model
GLP:	Not applicable
Type:	Not applicable
Year:	Not applicable
Media:	Air, Water, Soil, Sediment

Distributions:	Compartment	Released 100% to air	Release 100% to water	Release 100% to soil
	Air	3.99×10^{-14}	3.3×10^{-31}	7.07×10^{-29}
	Water	39.8	99.8	36
	Soil	60.2	4.98×10^{-16}	64
	Sediment	0.0753	0.189	0.0681
Conclusions:	EDTN is distributed primarily to water and soil.			
Reliability:	1			
Reference:	13			
Remarks:	When released equally to air, water and soil, EDTN is distributed 51.8% to water and 48.1% to soil.			
Additional References for Transport (Fugacity) Studies:	None			

3.4. *Biodegradation:*

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038
Method:	OECD 301
Type:	Modified Sturm Test
GLP:	Yes
Year:	1998
Degradation% after time:	0% at 28 days
Breakdown	Not determined
Products:	
Concentration Of	12 mg TOC/L
Test Chemical:	
pH Of Test Media:	7.8-8.1
Conclusions:	PDTN is not readily biodegradable.
Reliability:	1
Reference:	14
Remarks:	Source of test organism was activated sludge obtained from a municipal sewage treatment plant
Additional References for Biodegradation Studies:	None

4. Ecotoxicity

4.1. *Acute Toxicity to Fish:*

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038
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Method:	203
Type:	Static
GLP:	Yes
Year:	1998
Species/Strain:	Zebra fish/Teleostie, Cyprinidae
Supplier:	Charles River Aquatics, The Netherlands
Analytical Monitoring:	Gas Chromatography
Exposure Period:	96 hours
Nominal/Measured Concentrations:	100 mg/L; 107-109 mg/L
LC50:	>100 mg/L
Conclusions:	The LC50 of PDTN in zebra fish is >100 mg/L.
Reliability:	1
Reference:	15
Remarks:	There was no mortality during the study. Ten fish were used in the test group. The water hardness was 250 mg/CaCO ₃ /L. The pH was 7.2-8.2. The temperature was 20.7-21.3°C. The DO was 4.7-9.
Additional References for Acute Toxicity to Fish Studies:	None

4.2. Acute Toxicity to Invertebrates:.

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038	
Method:	202	
Type:	Static	
GLP:	Yes	
Year:	1998	
Species/Strain	Daphnia magna/Crustacea, Cladocera	Strauss, 1820
Supplier:	Not available	
Analytical Monitoring:	Gas Chromatography	
Exposure Period:	48 hours	
Nominal/Measured Concentrations:	1, 10, 100 mg/L; 110 mg/L	
EC50:	>100 mg/L	
Conclusions:	The EC50 of PDTN in Daphnia magna is >100 mg/L.	
Reliability:	1	
Reference:	16	

Remarks:	There was no mortality during the study. Ten fish were used at 1 and 10 mg/L and 20 fish in the 100 mg/L group. The water hardness was 250 mg/CaCO ₃ /L. The pH was 8.0-8.3. The temperature was 21.0-21.3°C. The DO was 8.8-8.9.
Additional References for Acute Toxicity to Invertebrates Studies:	None

4.3. Acute Toxicity to Aquatic Plants:

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038
Method:	201
Type:	Growth Inhibition Test
GLP:	Yes
Year:	1998
Species/Strain/Supplier:	Selenastrum capricornutum/CCAP 278/4/Not available
Analytical Monitoring:	Gas Chromatography
Exposure Period:	72 hours
Nominal/Measured Concentrations:	10, 18, 32, 56, 100 and 180 mg/L/10.5, 34, 189
EC50:	Growth inhibition – 60 mg/L; Growth rate reduction – 129 mg/L
Conclusions:	The EC50 in algae for growth inhibition and growth rate reduction for PDTN is 60 and 129 mg/L, respectively.
Reliability:	1
Reference:	17
Remarks:	Three replicates of the test concentrations were done. The water hardness was Ca+Mg: 0.24 mmol/L (24 mg CaCO ₃ /L). The pH was 8.1-8.4. The temperature was 21.2-23.0°C. The DO was 8.8-8.9.
Additional References for Acute Toxicity to Aquatic Plants Studies:	None

5. Mammalian Toxicity

5.1. Acute Toxicity:

5.1.1. Oral

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038
Method:	OECD 423
Type:	Acute Toxic Class Method
GLP:	Yes
Year:	1998
Species/Strain:	Rat/Wistar Cr1(WI)
Sex:	M/F
No. Of Animals Per	3
Sex Per Dose:	
Vehicle:	Polyethylene glycol
Route Of	Oral gavage
Administration:	
Time Of	15 Days
Observation	
Period:	
Doses	2000 mg/kg
Administered:	
LD50:	>2000 mg/kg
Conclusions:	The oral LD50 of PDTN in rats is greater than 2000 mg/kg.
Reliability:	1
Reference:	18
Remarks:	One female was found dead on day 3. Clinical signs of toxicity were lethargy, hunched posture, piloerection, diarrhea and red staining of the snout between days 1 and 3. Macroscopic examination showed hemorrhagic content of the urinary bladder in the animal that died. There were no effects in surviving animals.
Additional	None
References for	
Acute Oral	
Toxicity Studies:	

5.1.2. Dermal

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038
Method:	OECD 402
Type:	Acute Dermal
GLP:	Yes
Year:	1998
Species/Strain:	Rat/Wistar Cr1(WI)

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Sex:	M/F
No. Of Animals Per	5
Sex Per Dose:	
Vehicle:	Polyethylene glycol
Route Of	Dermal
Administration:	
Time Of	15 Days
Observation	
Period:	
Doses	2000 mg/kg for 24 hours
Administered:	
LD50:	>2000 mg/kg
Conclusions:	The dermal LD50 of PDTN in rats is greater than 2000 mg/kg.
Reliability:	1
Reference:	19
Remarks:	There was no mortality. Clinical signs of toxicity were red staining of the neck in one female between days 3 and 7 and scabs or scales in the treated area of two other females between days 3 and 6. Macroscopic examination showed no abnormalities.
Additional	None
References for	
Acute Dermal	
Toxicity Studies:	

5.1.3. Skin Irritation

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038
Method:	OECD 404
Type:	Semi-Occlusive
GLP:	Yes
Year:	1998
Species/Strain:	Rabbit/New Zealand white
Sex:	M
No. Of Animals:	3
Vehicle:	Water
Route Of	Dermal
Administration:	
Time Of Exposure:	4 hours
Time Of	1, 24, 48 and 72 hours
Observation	
Period:	
Concentration Of	0.5g
Test Material:	
Results:	There was no erythema or edema at any observation period.

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Conclusions:	PDTN was not irritating to rabbits following dermal exposure for 4 hours.
Reliability:	1
Reference:	20
Remarks:	None
Additional	None
References for Acute Dermal Irritation Studies:	

5.1.4. Sensitization

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038
Method:	OECD 406
Type:	Maximization Test
GLP:	Yes
Year:	1998
Species/Strain:	Guinea Pig/Dunkin Hartley
Sex:	F
No. Of Animals:	10
Vehicle:	Corn Oil
Route Of Administration:	Dermal
Time Of Observation Period:	24 Days
Concentration Of Test Material:	Induction: Day 1 – 0.1%; Day 8 – 50%; Challenge: Day 21 – 50%
Results:	There was no irritation seen 24 or 48 hours after challenge application.
Conclusions:	PDTN was not sensitizing to guinea pigs at a 50% challenge concentration.
Reliability:	1
Reference:	21
Remarks:	Alpha-hexylcinnamic aldehyde was the positive control.
Additional	None
References for Acute Dermal Sensitization Studies:	

5.2. Repeated Dose Toxicity:

Identity:	PDTN; CAS# 110057-45-9; Batch JNN98038
Method:	OECD 407
Type:	28-Day Oral Toxicity

GLP:	Yes
Year:	1998
Species/Strain:	Rat/Wistar Cr1(WI)BR
Sex:	M/F
No. Of Animals Per	20
Sex Per Dose:	
Vehicle:	Polyethylene glycol
Route of	Oral gavage
Administration:	
Time of	28 Days
Observation	
Period:	
Doses	50, 200,1000 mg/kg/day
Administered:	
Frequency of	Once daily for 28 days, 7 days per week
Treatment:	
NOAEL (NOEL):	200 mg/kg
LOAEL (LOEL):	1000 mg/kg
Toxic Response By	1000 mg/kg: Mortality – one female on day 23; Clinical
Dose Level:	signs – piloerection, hunched posture, severe brown staining of the fur, red discoloration of the urine of females; Clinical chemistry – Significant increase in alanine aminotransferase activity of males and females; Macroscopic exam - enlarged kidney and urinary bladder in female that died during the study; Organ weights – a minor significant increase in liver to body weight ration in males at 1000 mg/kg/day; Microscopic exam – minimal to slight centrilobular hepatocellular hypertrophy in males and females at 1000 mg/kg/day, female that died during the study had marked hydronephrosis, moderate tubular dilation and pyelonephritis and moderate inflammation of the urinary bladder. 200 mg/kg/day: Clinical signs – severe brown staining of the fur. 50 mg/kg/day: None
Conclusions:	PDTN administered daily by oral gavage to rats for 28 days resulted in signs of liver toxicity at 1000 mg/kg/day. The effects on the liver included an increased liver weight and alanine aminotransferase activity and microscopical changes. The NOAEL was 200 mg/kg/day.
Reliability:	1
Reference:	22
Remarks:	None
Additional	None
References for	
Repeated Dose	
Toxicity Studies:	

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5.3. Genetic Toxicity:

5.3.1. *In Vitro* Gene Mutations

Identity: PDTN; CAS# 110057-45-9; Batch JNN98038
Method: OECD 471/472
Type: Ames Test
GLP: Yes
Year: 1998
Cell Type: Salmonella typhimurium TA1535, TA1537, TA98, TA100;
E.coli WP2uvrA
Metabolic Activation: Rat S9 induced by Aroclor 1254
Concentrations: Without S9: 3, 10, 33, 100, 333, 1000, 3330, 5000
Tested: With S9: 100, 333, 1000, 3330, 5000
Vehicle: Dimethyl sulfoxide
Cytotoxic Concentration: No toxicity at any concentration.
Genotoxic Effects With Metabolic Activation: None
Genotoxic Effects Without Metabolic Activation: None
Conclusions: PDTN was not mutagenic in Salmonella typhimurium strains TA1535, TA1537, TA98, TA100 or E.coli strain WP2uvrA in the presence or absence of metabolic activation.
Reliability: 1
Reference: 23
Remarks: The test concentrations were tested in triplicate.
Additional: None
References for In Vitro Gene Mutation Studies:

5.3.2. *In Vitro* Chromosome Aberrations

Identity: PDTN; CAS# 110057-45-9; Batch JNN98038
Method: OECD 473
Type: In Vitro
GLP: Yes
Year: 1998
Cell Type: Cultured peripheral human lymphocytes
Metabolic Activation: Rat S9 induced by Aroclor 1254
Concentrations: Without S9: 333, 1000, 3330 (24 and 48 hour treatment)

Tested:	With S9: 100, 333, 1000, 3330, 5000 (3 hour treatment)
Vehicle:	Dimethylsulfoxide
Cytotoxic	No toxicity at any concentration.
Concentration:	
Genotoxic Effects	None
With Metabolic	
Activation:	
Genotoxic Effects	None
Without Metabolic	
Activation:	
Conclusions:	PDTN was not clastogenic in cultured peripheral human lymphocytes in the presence and absence of metabolic activation.
Reliability:	1
Reference:	24
Remarks:	The test concentrations were tested in duplicate.
Additional	None
References for <i>In Vitro</i> Chromosome Aberration Studies:	

References

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- 1 Determination Of The Melting Temperature Of PDTN. NOTOX Project No. 234822
11/19/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
 - 2 EPIWIN 3.10 U.S. Environmental Protection Agency 2000
 - 3 EPIWIN 3.10 U.S. Environmental Protection Agency 2000
 - 4 Determination Of The Density Of PDTN. NOTOX Project No. 234844
10/21/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
 - 5 Determination Of The Vapour Pressure Of PDTN. NOTOX Project No. 234855
10/21/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
 - 6 EPIWIN 3.10 U.S. Environmental Protection Agency 2000
 - 7 Determination Of The Partition Coefficient (N-Octanol/Water) Of PDTN.
NOTOX Project No. 234855 10/21/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
 - 8 EPIWIN 3.10 U.S. Environmental Protection Agency 2000
 - 9 Determination Of The Water Solubility Of PDTN.
NOTOX Project No. 234877 11/2/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
 - 10 EPIWIN 3.10 U.S. Environmental Protection Agency 2000
 - 11 EPIWIN 3.10 U.S. Environmental Protection Agency 2000
 - 12 Determination Of The Hydrolysis Of PDTN As A Function Of pH.
NOTOX Project No. 258582 4/9/99. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
 - 13 EPIWIN 3.10 U.S. Environmental Protection Agency 2000
 - 14 Determination Of 'Ready' Biodegradability: Carbon Dioxide (CO₂) Evolution Test
(Modified Sturm Test) With PDTN. NOTOX Project No. 235057 9/11/98.
Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
 - 15 96-Hour Acute Toxicity Study In Zebra-Fish With PDTN (Static).
NOTOX Project No. 235068 10/29/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
 - 16 Acute Toxicity Study In Daphnia Magna With PDTN (Static).
NOTOX Project No. 235079 10/29/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
 - 17 Fresh Water Algal Growth Inhibition Test With PDTN.
NOTOX Project No. 235081 10/29/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands

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- 18 Assessment Of Acute Oral Toxicity With PDTN In The Rat (Acute Toxic Class Method).
NOTOX Project No. 234967 9/23/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
- 19 Assessment Of Acute Dermal Toxicity With PDTN In The Rat.
NOTOX Project No. 234978 9/23/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
- 20 Primary Skin Irritation/Corrosion Study With PDTN In The Rabbit
(4-Hour Semi-Occlusive Application). NOTOX Project No. 234989 9/23/98.
Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
- 21 Assessment Of Contact Hypersensitivity To PDTN In The Albino Guinea Pig (Maximization-Test).
NOTOX Project No. 235002 10/26/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
- 22 Subacute 28-Day Oral Toxicity With PDTN By Oral Gavage In The Rat.
NOTOX Project No. 235024 11/19/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
- 23 Evaluation Of The Mutagenic Activity Of PDTN In The Salmonella Typhimurium Reverse
Mutation Assay And the Escherichia Coli Reverse Mutation Assay (With Independent Repeat).
NOTOX Project No. 235035 9/7/98. Sponsor: Akzo Nobel Chemicals B.V. The Netherlands
- 24 Evaluation Of The Ability Of PDTN To Induce Chromosome Aberrations In Cultured
Peripheral Human Lymphocytes. NOTOX Project No. 235046 10/30/98.
Sponsor: Akzo Nobel Chemicals B.V. The Netherlands